

CHAPTER 3

BIOELECTROMAGNETICS AND NUMERICAL TECHNIQUES

3.1 Introduction

The study of the interaction between microwave and biological tissue is often referred to as a complicated subject due to the complex nature of biological parts. In order to understand the effects of microwaves on biological tissues, it is necessary to determine the magnitude of the exposed fields within the particular organ. The effects of the interaction of microwave radiation with biological tissues during MWA can be considered as a result of three phenomena [172]: penetration of EM waves into the living system and their propagation into it, primary interaction of the waves with biological tissues, and the possible secondary effects induced by the primary interaction.

Microwave ablation (MWA) uses microwave frequencies, 915 MHz and 2.45 GHz to heat the tissue to lethal temperatures. With the development of the applications of microwaves in MWA, microwaves are used to treat larger and deep-seated tumors in shorter period of time with less complication. As mentioned earlier, there are no Food and Drug Administration (FDA)-approved commercial MWA devices available currently; hence much effort needs to be done by the researchers in order to develop MWA devices for clinical use, which may result in more efficient treatment for the patients that may not be curable with surgery. Although clinical tests are battle field for evaluating the performance of these devices, but are risky, expensive, time consuming, and limited in scope. However, theoretical models play a crucial role in MWA, because of its simplicity and versatility to develop and optimize the devices for validation. The

theoretical analysis may be divided into analytical methods and computational methods. The analytical methods are biased towards analytical solution of the wave equation; as a result, these methods are applicable only to objects with regular shapes, low frequency and homogeneous dielectric, except for few cases. Computational methods for the simulation of microwave ablation treatment are invaluable tools. The complex geometries and tissue properties involved in simulation of MWA, especially blood perfusion, makes computer simulations an ideal choice over analytical solutions which require many simplifying assumptions [189].

The ultimate goal of computer models for microwave tissue ablation is to induce tissue damage, which is a function of the time-temperature, and for this accurate prediction of the temperature profile in tissue is also necessary. The temperature profile in tissue during an ablation procedure depends upon two physical phenomena [190]:

- Interaction of microwaves with tissue
- Heat transfer in tissue

3.2 Interaction of Microwaves with Tissue

The electric and magnetic fields \mathbf{E} and \mathbf{H} were originally defined to account for forces; hence, the fundamental interactions of \mathbf{E} and \mathbf{H} with biological tissue are the forces exerted on the charges in the tissue. The electric fields are associated with forces in the presence of electric charges whereas the magnetic field exists as a result of the movement of electric charges (electrical currents) [191]. These propagation and absorption of microwaves in tissue is basically governed by Maxwell's equations.

However, the interaction of microwaves with tissue is actually more complicated, because, time varying electric field creates induced dipoles, aligns the existing dipoles within the material, alters the bound-charge orientation, and forces the electric charges to form electric currents. Three parameters are defined to describe these effects

macroscopically, namely permittivity, conductivity and permeability [192]. In general, biological materials are composed of a complex mixture of water, ions, polar and non-polar molecules, proteins, lipids and others. Characteristics of the dielectric properties of such complex materials are heavily dependent on their actual composition and the environment, as well as EM frequency and temperature.

3.2.1 Maxwell's Equations

Maxwell equations, which govern all electromagnetic phenomena, are the mathematical tools for a rigorous and accurate study of interaction between microwave and tissue [193].

Maxwell's equations were first published by James Clark Maxwell in 1873, which mathematically describe the interdependence of the electric field and the magnetic field stated in equations 3.1-3.4.

$$\nabla \times \mathbf{E} = -\frac{\partial \mathbf{B}}{\partial t} \quad (\text{Faraday's Law}) \quad (3.1)$$

$$\nabla \times \mathbf{H} = \frac{\partial \mathbf{D}}{\partial t} + \mathbf{J} \quad (\text{Ampere's Law}) \quad (3.2)$$

$$\nabla \cdot \mathbf{B} = 0 \quad (\text{Gauss's Law, magnetic}) \quad (3.3)$$

$$\nabla \cdot \mathbf{D} = \rho \quad (\text{Gauss's Law, electric}) \quad (3.4)$$

Where, \mathbf{E} is electric field intensity (V/m), \mathbf{H} is magnetic field intensity (A/m), \mathbf{D} is electric flux density (C/m^2), \mathbf{B} is magnetic flux density (Wb/m^2), \mathbf{J} is electric current density, $\partial \mathbf{D} / \partial t$ is displacement current, ρ is the electric charge density.

In addition there are three relations that concern the characteristics of the medium in which they exist. These relations are:

$$\mathbf{D} = \epsilon \mathbf{E} \quad (3.5)$$

$$\mathbf{B} = \mu \mathbf{H} \quad (3.6)$$

$$J = \sigma E \quad (3.7)$$

Where σ is the electric conductivity of the surrounding medium (S/m), ε is the electric permittivity (F/m) and μ is the magnetic permeability (H/m) of the surrounding medium. In free space:

$$\varepsilon = \varepsilon_o = 8.854 \times 10^{-12} (F / m) \quad (3.8)$$

$$\mu = \mu_o = 4\pi \times 10^{-7} (H / m) \quad (3.9)$$

In a material medium:

$$\varepsilon = \varepsilon_r \varepsilon_o \quad (3.10)$$

$$\mu = \mu_r \mu_o \quad (3.11)$$

Where, ε_r is the relative permittivity, or dielectric constant and μ_r is the relative permeability.

All EM waves are time-dependent electromagnetic fields and obey the above Maxwell's equations. If the EM waves are time-harmonic fields with sinusoidal time-variations, they have the form as:

$$E(t) = E_o \cos(\omega t + \varphi_E) \quad (3.12)$$

$$H(t) = H_o \cos(\omega_o + \varphi_H) \quad (3.13)$$

Where, ω is the angular frequency (rad), φ_E is the initial phase of E and φ_H is the initial phase of H.

The Maxwell's equations may then be expressed in phasor form as:

$$\nabla \times E = -j\omega B \quad (3.14)$$

$$\nabla \times H = j\omega D + J \quad (3.15)$$

$$\nabla \cdot B = 0 \quad (3.16)$$

$$\nabla \cdot D = \rho \quad (3.17)$$

If vacuum is considered as the medium, the equations can be transformed into the wave equations called as Helmholtz equations given by [154]:

$$\nabla^2 \mathbf{E} + \omega^2 \mu \epsilon \mathbf{E} = 0 \quad (3.18)$$

$$\nabla^2 \mathbf{H} + \omega^2 \mu \epsilon \mathbf{H} = 0 \quad (3.19)$$

where ϵ and μ are complex tensors in the Helmholtz equations. These two equations are uncoupled. Only one of the two equations needs to be solved in order to completely describe the whole problem.

3.2.2 EM Waves in Material Medium

In general, material properties of the medium ϵ_r , μ_r and σ are functions of the position, direction, field strength, and frequency of the applied field. The majority of the material can be assumed to be homogeneous (material properties independent of position), isotropic (material properties independent of direction), and linear (material properties independent of field strength) over sufficiently large values of field strength and broad range of frequency, may be called simple, but most of the material are nonmagnetic with $\mu_r=1$. Good conductors are described by a high value of σ , which is constant from dc up to the infrared (IR) frequencies, their permeability and permittivity are approximately equal to that of vacuum. For perfect dielectrics the value of σ is characterized as unity. For non simple materials, ϵ and μ are described by dielectric and permeability tensors, respectively.

If the medium is conductive with $\sigma \neq 0$, the wave equation becomes:

$$\nabla^2 \mathbf{E} + \omega^2 \mu \epsilon \left(1 - j \frac{\sigma}{\omega \epsilon}\right) \mathbf{E} = 0 \quad (3.20)$$

Considering the wave traveling in the z direction only, one possible solution is:

$$\mathbf{E} = \mathbf{E}_0 e^{-j\gamma z} \quad (3.21)$$

Where γ is the wave propagation constant, which is given as:

$$\gamma = \alpha + j\beta = \sqrt{j\omega\mu(\sigma + j\omega\epsilon)} = j\omega\sqrt{\mu\epsilon} \sqrt{1 - j \frac{\sigma}{\omega\epsilon}} \quad (3.22)$$

Where α is the attenuation constant (Np/m) and β is the phase constant (rad/m) and

$$\alpha = \frac{\omega\sqrt{\mu\epsilon}}{\sqrt{2}} \left[\sqrt{1 + \left(\frac{\sigma}{\omega\epsilon}\right)^2} - 1 \right]^{1/2} \quad (3.23)$$

$$\beta = \frac{\omega\sqrt{\mu\epsilon}}{\sqrt{2}} \left[\sqrt{1 + \left(\frac{\sigma}{\omega\epsilon}\right)^2} + 1 \right]^{1/2} \quad (3.24)$$

The phase velocity v_p and wavelength λ are functions of frequency as:

$$v_p = \frac{\omega}{\beta} = \frac{\sqrt{2}}{\sqrt{\mu\epsilon}} \left[\sqrt{1 + \left(\frac{\sigma}{\omega\epsilon}\right)^2} - 1 \right]^{1/2} \quad (3.25)$$

$$\lambda = \frac{2\pi}{\beta} = \frac{\sqrt{2}}{f\sqrt{\mu\epsilon}} \left[\sqrt{1 + \left(\frac{\sigma}{\omega\epsilon}\right)^2} - 1 \right]^{1/2} \quad (3.26)$$

The solution of E in phasor form can be written as:

$$E(z) = E_o e^{-\alpha z} e^{-j\beta z} \quad (3.27)$$

The time-dependent form of E is:

$$E_x(z, t) = E_o e^{-\alpha z} \cos(\omega t - \beta z + \phi_E) \quad (3.28)$$

For perfect dielectric medium in which $\sigma = 0$, it can be deduced that:

$$\alpha = 0 \quad (3.29)$$

$$\beta = \omega\sqrt{\mu\epsilon} = \omega\sqrt{\mu_r\mu_o\epsilon_r\epsilon_o} \quad (3.30)$$

$$v_p = \frac{\omega}{\beta} = \frac{1}{\sqrt{\mu_r\mu_o\epsilon_r\epsilon_o}} \quad (3.31)$$

$$\lambda = \frac{2\pi}{\beta} = \frac{1}{f\sqrt{\mu_r\mu_o\epsilon_r\epsilon_o}} \quad (3.32)$$

For an imperfect dielectric medium with $\sigma \neq 0$ but, $\sigma/\omega\epsilon \ll 1$ it can be shown that:

$$\alpha \approx \frac{\sigma}{2} \sqrt{\frac{\mu}{\epsilon}} \quad (3.33)$$

$$\beta \approx \omega \sqrt{\mu\epsilon} \quad (3.34)$$

$$v_p = \frac{\omega}{\beta} = \frac{1}{\sqrt{\mu\epsilon}} \quad (3.35)$$

$$\lambda \approx \frac{1}{f \sqrt{\mu\epsilon}} \quad (3.36)$$

Further, for a medium in which $\sigma/\omega\epsilon \gg 1$, the corresponding propagation parameters become:

$$\alpha \approx \sqrt{\pi f \mu \sigma} \quad (3.37)$$

$$\beta \approx \sqrt{\pi f \mu \sigma} \quad (3.38)$$

$$v_p \approx \sqrt{\frac{4\pi f}{\mu \sigma}} \quad (3.39)$$

$$\lambda \approx \sqrt{\frac{4\pi}{f \mu \sigma}} \quad (3.40)$$

The quantity $\sigma/\omega\epsilon$ is called the loss tangent and describes how lossy the medium is. If the loss tangent $\sigma/\omega\epsilon \ll 0.1$, the medium is called a good dielectric material. If the loss tangent $\sigma/\omega\epsilon \gg 10$, the medium is called a good conductor.

3.2.3 Depth of Penetration

In good conductors, the fields attenuate very rapidly. Skin depth, or depth of penetration, is an alternative way to characterize a medium with non zero conductivity. Skin depth is defined as the distance over which the fields are attenuated by a factor of e^{-10} :

$$\text{Skin Depth} = \delta = \frac{1}{\alpha} = \frac{1}{\sqrt{\pi f \mu \sigma}} \quad (3.41)$$

The skin depth of a good conductor is very small, especially at high frequencies, causing currents to reside near the conductor's surface. The containment of current reduces the effective cross-sectional area of the conductor and therefore increases conduction loss. A general medium is referred to as a material that is neither a good dielectric nor a good conductor. For a general medium, it follows:

$$10 > \frac{\sigma}{\omega\epsilon} > 0.1 \quad (3.42)$$

3.2.4 Poynting Vector and Power Flow

When an electromagnetic wave propagates in a medium, it carries power along with it. The instantaneous power density at any location in the medium is given by the Poynting vector, defined as:

$$\mathbf{P}(t) = \mathbf{E}(t) \times \mathbf{H}(t) \quad (3.43)$$

The time-average power flow density for time-varying fields is given by:

$$\langle P(t) \rangle = \frac{1}{T_0} \int_0^{T_0} P(t) dt = \frac{1}{T_0} \int_0^{T_0} \mathbf{E}(t) \times \mathbf{H}(t) dt \quad (3.44)$$

Where T_0 is the period of the EM wave. In a lossy medium, the field \mathbf{E} and \mathbf{H} are attenuated as the factor of $e^{-j\alpha z}$ and the power density is attenuated as the factor of $e^{-2j\alpha z}$

3.2.5 Dielectric Properties of Biological Tissues

The dielectric properties of a biological tissue result from the interaction of electromagnetic radiation with its constituents at the cellular and molecular level. The applied \mathbf{E} field causes induced-polarization, alignment of already existing electric dipoles, and movement of free charges. The electric fields inside and outside of the substance are altered from the incident field because of these effects [194].

Three macroscopic terms are defined to account for the interactions between EM fields and matters. Permittivity ϵ (F/m, Farads per meter), describes how much induced

polarization and partial alignment of permanent electric dipoles occurs for a given applied E field. Conductivity σ (S/m, Siemens per meter), describes how much conduction current density is produced by a given applied E field. Alignment of permanent magnetic dipoles is accounted for by permeability μ (H/m, Henry per meter).

The dielectric properties of materials are obtained from their measured complex relative permittivity, $\hat{\epsilon}$ expressed as:

$$\hat{\epsilon} = \epsilon' + j\epsilon'' \quad (3.45)$$

Where ϵ' is the relative permittivity of the material and ϵ'' is the out-of-phase loss factor associated with it such that

$$\epsilon'' = \frac{\sigma}{\epsilon_0} \omega \quad (3.46)$$

Where σ is the total conductivity of the material which, depending on the nature of the sample, may include a contribution from a frequency-independent ionic conductivity, σ_i . In this expression, ϵ_0 is the permittivity of free space and ω the angular frequency of the field. The dielectric properties are determined by ϵ' and ϵ'' values, or ϵ' and σ values, as a function of frequency. The dielectric properties of tissues vary with microwave frequency, the corresponding relationship between dielectric properties and microwave frequency for different types of biological tissues has been summarized by Gabriel [195-197].

Gabriel suggested the empirical parameterized equation to approximate the measured dielectric properties of different tissues. By using the suggested parameters to different tissue types, the complex relative permittivity of tissues could be calculated as [198]:

$$\hat{\epsilon}(\omega) = \epsilon_\infty + \sum_n \frac{\Delta\epsilon_n}{1+(j\omega\tau_n)^{1-\alpha_n}} + \frac{\sigma_i}{j\omega\epsilon_0} \quad (3.47)$$

The parameters considered for liver tissues by Gabriel are as given in Table 3.1. ϵ_∞ is the relative permittivity at infinite frequency, $\Delta\epsilon$ is magnitude of dispersion, α_n is a attenuation constant, σ_i is the static ionic conductivity, and τ_n is the n^{th} relaxation time constant.

Table 3.1: Parameters for liver tissue for Gabriel tissue dielectric equation

Parameter	Value	Parameter	Value
ϵ_∞	4.0	σ_i	0.0200
$\Delta\epsilon_1$	39.0	$\Delta\epsilon_2$	6000
$\tau_1(ps)$	8.84	$\tau_2(ns)$	530.52
α_1	0.10	α_2	0.20
$\Delta\epsilon_3$	5.0×10^4	$\Delta\epsilon_4$	3.0×10^7
$\tau_3(\mu s)$	22.74	$\tau_4(ms)$	15.915
α_3	0.20	α_4	0.05

The dielectric properties of biological tissues are also dependent on temperature changes because, temperature dependent dielectric property changes the tissue water and protein contents. When the temperature increases above 60°C , protein denaturization takes place due to which changes in dielectric properties are irreversible. For reversible changes, the temperature coefficients were found to be $1.82 \pm 0.28\% \text{ }^\circ\text{C}^{-1}$ for conductivity and $-0.130 \pm 0.0059\% \text{ }^\circ\text{C}^{-1}$ for relative permittivity respectively [199-202]. Hence dielectric properties are function of temperature as well as the time for which the elevated temperature is maintained. It is worth mentioning here that measuring dielectric at elevated temperature is difficult task, as dielectric properties are also depends upon water content. Soft tissues generally contain 75% water (containing salt), and this water-salt solution is responsible for the dielectric properties of the tissue. When the water evaporates at high temperatures, the tissue gets more dessicated with lower relative permittivity and conductivity. As the liver contains large amount of water, the dielectric properties of liver tissue are considered similar to those of water at 2.45 GHz. When the water gets evaporated, the liver tissue becomes less lossy, which

results in greater penetration of microwaves. That's why the radiation pattern and impedance matching of antenna therefore may change substantially during the course of ablation.

3.3 Heat Transfer in Tissue

Once the electric field goes straight through the body tissues, the electromagnetic energy turns into heat due to dielectric losses. This means that, as long as the electric field travels across the human body, it decreases its energy and increases the temperature in surrounding tissues. The transportation of thermal energy in biological tissue is a complex process, the increase in temperature within the human body when electromagnetic energy is present is influenced by other phenomena such as conduction, convection, radiation, metabolism heat generation, thermal migration, blood perfusion, tissue water evaporation, condensation, etc. It is very difficult to study such a complex process; especially when behavior of tissue is unpredictable, at high temperatures. Unfortunately, MWA is one of the thermal ablative technologies which heats the tissue to a high temperature enough for all the phenomena to happen.

3.3.1 Specific Absorption Rate (SAR)

The specific absorption rate (SAR) is used in dosimetry to denote the transfer of energy from the EM fields to biological tissue (rate of energy deposition per unit mass of tissue). The SAR is defined as the rate of change of energy absorbed by charged particles within an infinitesimal volume at that point within an absorber, averaged by the mass of that small volume or the rate at which energy is deposited in any kind of material per unit of mass; that is, the power absorbed by the tissue per unit of mass. Thus, SAR is the parameter employed to quantify the electromagnetic magnitude and its absorption inside biological tissues. In other terms, SAR can be seen as the velocity at which the human body absorbs the electromagnetic energy [203].

$$SAR = \frac{\partial w / \partial t}{\rho} \quad (3.48)$$

However, the rate of change of energy $\partial W / \partial t$ is equivalent to power density (P). Hence the above equation can be rewritten as:

$$SAR = \frac{P}{\rho} \quad (3.49)$$

Re-formulated equation to relate the SAR to internal E fields becomes:

$$SAR = \frac{\sigma}{\rho} |E|^2 \quad (3.50)$$

Where ρ is the electric charge density, σ is the electric conductivity, E is the electric field intensity. The scope of the SAR evaluation includes virtually all RF transmitting devices that are used in close proximity to the human body and transmit more than 20 mW of RF power [204-205] .

3.3.2 Bioheat Equation

The relationship between SAR and the resulting temperature rise is quite complex, and is dependent on many parameters. The traditional continuum heat-sink model, developed by Pennes [206], was found to give remarkable accurate results in many circumstances. For heat transfer in the tissue, the temperature profile in tissue during ablation is obtained by solving a bioheat equation. Hence Pennes bioheat equation is the most widely used bioheat equation for modeling thermal therapy procedures.

The Pennes' Bioheat equation effectively describes how heat transfer occurs in biological tissue and evaluates the rate of change of temperature due to the heat absorption.

$$\rho c \frac{\partial T}{\partial t} = \nabla \cdot k \nabla T + SAR - \rho_{b1} c_{b1} w_{b1} (T - T_{b1}) \quad (3.51)$$

Where T is the tissue temperature (K), ρ is the charge density for tissue (kg/m^3), c is specific heat capacity (J/kg.k), k is thermal conductivity (W/m.k), ρ_{b1} is blood density

(kg/m³), c_{bl} is the specific heat capacity of blood (J/kg.k), w_{bl} is blood perfusion rate (kg/m³.s), T_{bl} is blood temperature (K), SAR is the microwave power per unit volume applied by MWA (W/m³). Some important thermal and physical properties of normal liver tissue are as listed in Table 3.4.

The major physical phenomena considered in the Bioheat equation are microwave heating and tissue heat conduction. Heat conduction between tissue and blood flow in tissue is approximated by the term $\rho_{bl}c_{bl}w_{bl}(T - T_{bl})$ in the equation 3.51. Heat radiation and metabolism heat generation are assumed to be minimal during MWA and are ignored [207].

Table 3.2 Thermal and physical properties of liver tissue and blood

Expressions	Name	Values
Thermal Conductivity, liver	K_liver	0.56 [W/(kg*K)]
Density, blood	Rho_blood	1000[kg/m ³]
Specific heat, blood	C_blood	3639 [J/(kg*k)]
Blood perfusion rate	Omega_blood	3.6 e-3[1/s]
Dielectric permittivity	sig_liver	2.03
Thermal conductivity, liver	k_liver	1.69 [S/m]
Relative permittivity, liver	eps_liver	43.3 [F/m]
Blood Temperature	T_blood	37 [degC]
Blood Flow rate	F_blood	5X10 ⁻⁶ [m ³ /kg.s]

Since the Bioheat equation modeling of the heat transfer in perfused tissues cannot account for the actual thermal equilibration process between the flowing blood and the surrounding tissue, hence it does not cover convective heat transfer, tissue water evaporation and water vapor condensation. Although new models based on a more realistic anatomy of the perfused tissue are developed, but due to the lack of experiment grounding and inherent complexity, the Pennes model is still the best practical approach for modeling Bio-heat transfer in living tissue. When applied under valid conditions, the Bioheat equation has proved to be a viable approximation for heat transfer in biological tissues [208-212].

3.3.3 Blood Perfusion and Effects

The effects of blood flow on heat transfer in biological tissue must be considered when thermal ablations are performed in-vivo to living tissues. A common approach for small blood vessels is to consider them as uniformly distributed heat sinks in the whole tissue, based on the basic assumption that blood enters the local tissue volume at the arterial temperature T_{b1} and leaves this volume at local tissue temperature [213].

The effect of blood perfusion and specific heat are depicted by the term $\rho_{b1}c_{b1}w_{b1}(T - T_{b1})$ of bioheat equation.

An alternative method to treat small vessel blood flow is to use the concept of effective thermal conductivity k_{eff} , instead of the concept of heat sink as given by following equation [27].

$$\rho c \frac{\partial T}{\partial t} = \nabla \cdot k_{eff} \nabla T + SAR \quad (3.52)$$

Large blood vessels cannot be treated as uniform heat sinks or enhanced thermal conductivity. They have to be considered individually because convective heat transfer inside the blood vessel cannot be ignored [213-214].

3.3.4 Thermal Properties and Dependent Factors

Tissue thermal and physical properties are generally not constant. Temperature and tissue composition are two of the most important factors that could affect tissue properties. Researchers have reported on the relationship between these affecting factors and tissue properties.

Bhattacharya studied the temperature dependence of thermal conductivity ex-vivo with cow liver in 2003 [215]. He showed that thermal conductivity of cow liver had reversible temperature dependence for temperatures up to 90°C. The change with

thermal conductivity was irreversible if temperature was over 90°C. His results showed that:

$$k(T) = 0.4475 + 0.0033T \quad (3.53)$$

Where k is the tissue thermal conductivity and T is the temperature. Bhattachary's equation was good for $25^\circ\text{C} < T < 80^\circ\text{C}$. The temperature coefficient was higher than the previous results on human liver by Valvano 1985 [216]:

$$k(T) = 0.4692 + 0.0012T \quad (3.54)$$

Valvano's results were good for $3^\circ\text{C} < T < 45^\circ\text{C}$

According to Bhattacharya, the thermal conductivities of cow liver are 0.57 and 0.74 for temperatures at 37.5°C and 90°C respectively. The accuracy of the empirical equation is still questionable, especially for the situation that the temperature coefficients are different for different tissue types and from in-vivo to ex-vivo, but the temperature dependence of tissue thermal conductivity is confirmed.

Similar to the tissue water content dependence of tissue dielectric properties, tissue thermal properties also depend on the tissue water content. Empirical equations are available to calculate tissue thermal properties from tissue water content. Duck has summarized results from different researchers in [217].

3.3.5 Thermal Responses of Biological Tissues during MWA

When microwave power is applied the tissue near the active radiation region absorbs more microwave wave energy which elevates the tissue temperature. Although heat is also transferred from tissue at higher temperature to tissue at lower temperature by thermal conduction and blood perfusion in the liver tissue but the overall effect of the microwave power is to raise tissue temperature in a limited region. To determine the clinical meaningful thermal dose is a serious problem in thermal therapy. However

thermal dose may be defined as the length of exposure of a particular body part to a particular temperature.

3.3.5.1 Tissue Responses versus Temperature

The most commonly used model to describe the tissue thermal damage mathematically is the Arrhenius model [218]. It has been shown that there is an exponential relationship between the necessary treatment time and temperature to cause tissue damage for many tissue types. In the Arrhenius model temperature at 43°C represents the “break” point [219].

Every increase of temperature by 1°C above 43°C, treatment duration cuts to half to cause tissue damage. This relationship is consistent with laboratory data, proven for a variety of cell lines with a wide range of temperature sensitivities [220].

The rule can be mathematically described by the isoeffect equation:

$$t_1 = t_2 \times R^{T_1 - T_2} \quad (3.55)$$

Where t_1 and t_2 are the necessary treatment durations at temperatures T_1 and T_2 respectively, R is constant, equal to 0.5 for temperatures above 43°C and 0.25 for temperatures below 43°C [221]. Sapareto and Dewey suggested to quantify the thermal damage by a thermal dose-cumulative equivalent minutes at 43°C, as the parameter CEM_{43} .

$$CEM_{43} = \int R^{43 - T(t)} dt \quad (3.56)$$

Once the thermal dose exceeds a certain limit, the tissue is considered to be damaged.

The critical value of thermal dose is about 340 min for liver tissue [222].

Figure 3.1 shows that the critical treatment time required to cause tissue damage, depends on the temperature, assuming the treatment temperature is constant through the whole treatment duration. To damage liver tissue, the duration needs to be 340 min for temperature at 43°C, 5.3 min for temperature at 49°C, 1.3 min for temperature at 51°C.

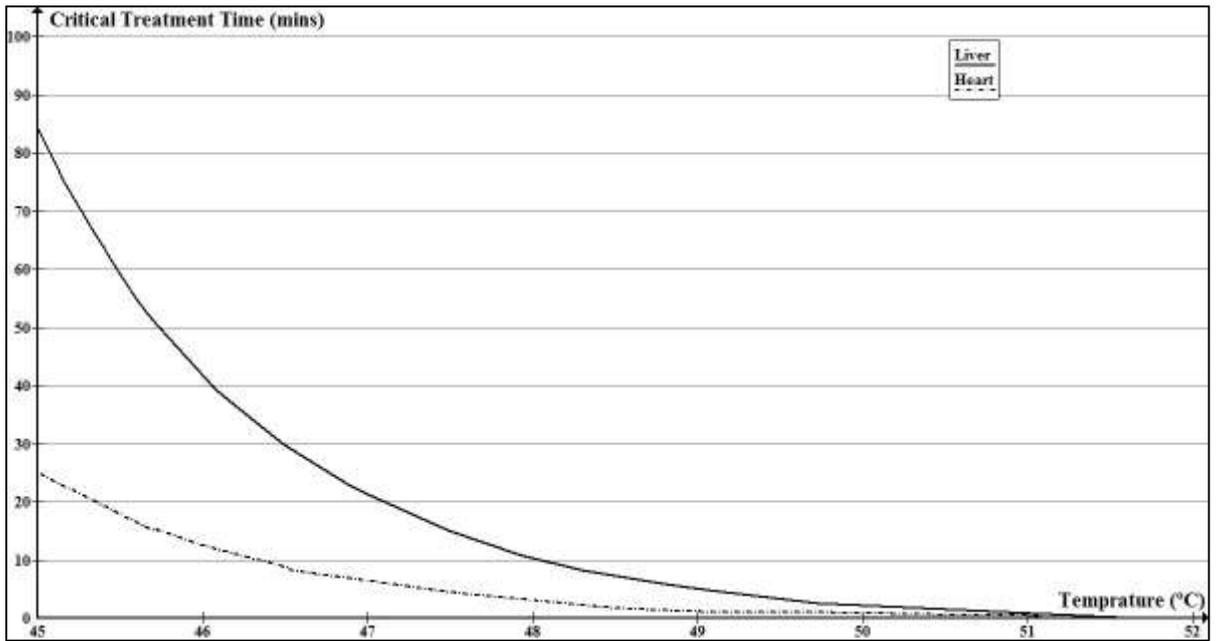


Figure 3.1: Treatment duration versus treatment temperature

3.3.5.2 Thermal Measurements

It is very important to make accurate thermal measurements in human beings. There are several thermometric methods available for the temperature measurement due to microwaves, however only a few are commercially available.

The rate of temperature change in the subcutaneous tissue in vitro exposed to EM radiation is related to SAR by Deshan yang as [154]:

$$\frac{\Delta T}{\Delta t} = \frac{(SAR + P_m - P_c - P_b)}{c} \quad (3.57)$$

Where ΔT is the temperature increase, Δt is the exposure duration, P_m is the metabolic heating rate, P_c is the rate of heat loss per unit volume due to thermal conduction, P_b is the rate of heat loss per unit volume due to blood flow, and c is the specific heat. If before the exposure a steady-state condition exists i.e $P_m = P_c + P_b$, then during the initial period of exposure equation gets reduced to:

$$\frac{\Delta T}{\Delta t} = \frac{\text{SAR}}{c} \quad (3.58)$$

3.4 Thermometry Techniques

The clinical invasive thermometry techniques used for measurement of temperature are highly accurate with high temporal and spatial resolution. For high-quality thermometry, the temperature probes are used to place at a target region in critical locations, however, it is time consuming, uncomfortable, and risky for the patient. Invasive thermometry can be accomplished generally by three types of electrodes: thermocouple sensors, thermistors, and optical fiber thermometers [172].

3.4.1 Thermocouple Sensors

Thermocouple is used widely as a thermometric sensor. In 1822, an Estonian physician named Thomas Seebeck discovered (accidentally) that when two wires with dissimilar electrical properties are joined at both ends and one junction is made hot and the other cold, a small electric current is produced proportional to the difference in the temperature is called Seebeck effect. There are two types of thermocouples: a sheath type and a protected tube type. Sheathed thermocouple probes are available with three junction types, i.e. grounded, ungrounded, or exposed. The protected-tube type thermocouple consists of a protected tube, a terminal box, and a glass that insulates the thermocouple wire. The thermocouples are having the advantage of combining multiple sensors in one probe, but the main disadvantage is its susceptibility to EM disturbances.

3.4.2 Thermistor

Temperature sensor called a thermistor is thermally sensitivity resistor, available with two types, a negative temperature coefficient (NTC) and positive temperature coefficient (PTC). NTC is manufactured from oxides of the transition metals – manganese, cobalt, copper and nickel, while PTC thermistors are manufactured from

Barium Titanate and should be chosen when a drastic change in resistance is required at a specific temperature range. Thermistors typically work over a relatively small temperature range, compared to other temperature sensors, and can be very accurate and precise within that range [223].

3.4.3 Optical Fiber Thermometer

In 1987, the first laser-based emissivity measuring infrared thermometer was introduced and used world widely in industrial and research applications. In 1990, a fiber-optic sensor version was developed. This provided broader temperature measurement ranges; smaller target sizes; lower cost; and most importantly, flexibility of sensor head size, shape, and materials. The optical fiber thermometer has a simple thermosensor attached to the tip of an optical fiber that is composed of a Phosphor capable of excitation by a light-emitting diode (LED). The tip of the optical fiber is attached to the measured object and a pulse of the infrared (IR) excitation light at a wavelength of 940 nm is applied. This applied pulse is converted into visible light at a wavelength of 550 nm, simultaneously it is modulated by the temperature. After the IR pulse is applied, there is an afterglow for a while, even if the exciting light is cut off. The afterglow is dependent on temperature. Therefore, the temperature can be calculated by sequential sampling of the quantity of afterglow in a time series and summing it, after the search of the afterglow integral luminance.

Currently, temperature sensors placed on the skin surface and inside invasively placed catheters within the treatment volume are the only reliable means available for acquiring detailed thermometry data. Manual mapping of various types of temperature sensors through phantoms, animal, and human tissues has been employed in order to characterize temperature distributions during treatments and to determine applicator SAR patterns. Commercially available thermometry equipment is inadequate in

providing the thermometry information needed to properly control these applicators at a reasonable cost. One method of increasing the amount of accessible temperature data is by spatially multiplexing the available thermometry by automatically scanning the sensors through catheters placed within the treatment field. Several investigators have used invasive techniques to measure temperature elevation during thermal therapy [224]. A list of invasive temperature measuring devices is given in Table 3.2

Table 3.3 Comparative list of invasive temperature measuring devices

Type	Description
Thermistors	Strong interaction with EM fields. Accurate when not used in EM fields.
Thermocouples	Multiple junction probes possible. Filtering and shielding required. Microjunction preferable.
Fiber Optics	No interaction with EM fields. Frequent calibration required.

3.5 Numerical Techniques Framework in MWA

Computational electromagnetics is the subject of numerically solving Maxwell's equations using limited computer resources. These solutions describe the physical interactions between the electromagnetic fields and objects exposed to the fields [225]. In bioelectromagnetics, numerical computer simulations are often used to calculate the electric and magnetic fields in the human body.

Numerical techniques basically discretize the complex configuration into small elements, or mathematical cells, each of which is assigned its own properties, such as conductivity and permittivity etc. By transforming the Maxwell's equations for solving the field equations, the physical approximations can be avoided or reduced to maintain high accuracy [86]. By increasing the number of elements, the discretized problem can be infinitely close to the original continuous problem. Therefore, the application of numerical methods is only limited by the speed and storage of computers [226].

To deal with a bioelectromagnetic problem, say an antenna in the vicinity of a human body, there is a dire need to find a numerical algorithm that can yield sufficiently accurate results without an excessive effort. In order to evaluate the effects of electromagnetic fields and temperature on the tissues of the human body, electromagnetic and thermal problems can be solved in some simplified models, like cylinders, as proposed in some documents or a real human body models [227-228]. To solve an electromagnetic or thermal problem by means of numerical analysis the main elements of the problem are:

- The numerical computational method
- The computational domain that includes the model describing the volume
- The field source

In bioelectromagnetics the computation methods are used to evaluate numerically the electric and magnetic field or the thermal field in order to assess the exposure of radiation to the people or their therapeutic effects, the choice of the method depends on the problem to be solved. OP Gandhi in 1995 [229] reviewed the numerical methods used in biological structures to solve bioelectromagnetic problems. Also, M. Stuchly [330] worked on the same field to evaluate the Interaction of low-frequency electric and magnetic fields with the human body. The numerical methods used to predict the induced fields in biological bodies of realistic shape and composition are enlisted below:

- Quasi-Static Impedance Method
- Methods of Moments (MoM)
- Finite Difference Time Domain Method (FDTD)
- Finite Element Method (FEM)

The quasi-static impedance method is restricted to lower frequencies, but the MoM, the FDTD and the FEM methods may be used for any frequency of interest. In addition, both the Finite Difference Time Domain Method and Finite Element Methods involve solving Maxwell's equations in the differential form for the computation of induced fields.

3.5.1 Quasi-Static Impedance Method

The impedance method was introduced in 1984 by Gandhi et al. [231] as a simulation method suitable for quasi-static electromagnetic radiation problems that arise in the field of bioelectromagnetics. For low frequency situations, where the dimensions of the biological body are small compared to the wavelength, the impedance method has been found to be highly efficient as a numerical procedure for calculating internal current densities and induced electrical fields. In this method, the biological body or the exposed part thereof is represented by three dimensional networks of impedances whose individual values are obtained from complex conductivities for various location of the body. The impedance method has been used for calculating SAR distribution for operator exposure to spatially variable fields of induction heater, linearly or circularly polarized RF magnetic fields representative of magnetic resonance imagers, due to capacitive type electrodes used for hyperthermia and for interstitial RF needle applicators for hyperthermia. The main limitation of this method is that it is restricted to frequencies <30 to 40 MHz for human body.

3.5.2 Method of Moments (MoM)

The MoM [115] is used in conjunction with either the volume integral equation method or the surface integral equation method for finding the solution to unknown fields inside the body, hence divided into two types:

- VMoM
- SMoM

3.5.2.1 VMoM

The volume integral equation method (VMoM) requires determination of unknown fields throughout the volume of the body using the volume equivalence principle and the MoM. In 1984, for the first time, the volume integral equations were solved using a modern conforming approaches i.e. MoM [232]. The MoM is used to transform the integral equation into a matrix equation by subdividing the body into N simply shaped cells. The fundamental limitation of this method is the use of full or nearly full matrix which needs the extensive computer storage and long running time. Even with the availability of larger and faster computers, this difficulty is not completely yet resolved.

3.5.2.2 SMoM

The surface integral equation method (SMoM) makes use of two coupled integral equations, i.e. electric field and magnetic field integral equations for the tangential components of the field of the surface separating the biological body from the air. The unknown surface currents are found by Fourier decomposition and moment method. The fields inside the biological body are calculated using the previously computed surface currents, the reciprocity theorem and the concept of measurement matrix. The surface integral equation method is applicable to any arbitrarily shaped homogeneous body of revolution.

MoM is efficient treatment for perfectly or highly conducting surfaces. Only the surface is meshed; no “air region” around the antenna needs to be meshed. For wire antennas, the treatment is even more efficient, since only a one-dimensional discretization of wire is undertaken. The MoM automatically incorporates the “radiation condition” – i.e. the correct behavior of field far from the source. This is very important

when dealing with radiation or scattering problem. The working variable in this technique is the current density, from which many important antenna parameters (impedance, gain radiation patterns, etc.) may be varied, some directly and some via straight forward numerical integration. By using Sommerfield potentials, efficient formulation may be derived for stratified (layered) media [233].

But the major disadvantage with the MoM is that it does not handle electromagnetically penetrable materials as well as differential equation formulations. This is especially true if the material is inhomogeneous. If the materials are homogeneous, a reasonably efficient fictitious, equivalent surface current formulation may be used, but inhomogeneous material require fictitious equivalent volumetric currents, and become very expensive computationally. The MoM does not scale gracefully with frequency- for typical applications requiring a surface mesh. Moreover some MoM formulations, in particular those based on the magnetic field integral equation (MFIE), require the surface to be closed, but this is impractical [234].

In conclusion, the MoM is preferred method for frequency domain radiation and scattering problems involving perfectly or highly conducting wires and/or surfaces. If the problem involves inhomogeneous dielectric materials, it is unlikely to be the best formulation, but if hybridized with FEM a very efficient formulation can result.

3.5.3 Finite Difference Time Domain Method (FDTD)

The FDTD method was first proposed by K.S Yee in 1966 [114] but sprang to prominence in the 1980s and has proved to be very efficient numerical algorithm in computational electromagnetics for the solution of Maxwell's curl equations. There were two technological driving factors behind this, on one hand, increasing interest in modeling of inhomogeneous materials, in particular for the assessment of human exposure to RF fields, and the other is the development of low observable stealth

technology. This method is based on the approximation of the derivative by central differences to evaluate the field components. The traditional FDTD algorithm generates regular grid in the Cartesian co-ordinate system and uses staircase approximation to analyze structure on an underlying Cartesian grid. The development by Berenger of perfectly matched layer in 1994 solved the previously problematic issue of mesh termination and removed the last hurdle to the widespread adoption of the method. In the new millennium, with desktop PCs with hundreds of megabytes available at relatively low cost, the FDTD method has been established as one of the most popular method in CEM, both in industry and academia. The apparent simplicity of the basic implementation also means that it is very popular with research community, where “do-it-yourself” FDTD codes are commonly encountered.

FDTD can be used to solve many types of electromagnetic problems, as cost of computing keeps reducing. The method can be applied to antenna design and analysis, microwave circuits, biological interaction with electromagnetic waves, optics and radar cross-section problems. The method handles the solution of interaction of antennas with the human body in a straight forward manner for prediction of biomedical applications, such as electromagnetic heating for cancer [135, 235].

The reduction of the equations and of the boundary or interface conditions defined in the continuous domain, to the discretized equations valid for the nodes, is performed by means of various algorithms which replace derivatives and integrals with divided difference approximations obtained as functions of nodal values. This can be accomplished, for instance, by using interpolating functions, which are not defined in specific sub domains but simply at their neighboring nodes. As a consequence, severe difficulties are encountered in solving many problems using finite difference technique, and therefore, their efficiency is considerably limited. This is essentially due to

geometrically reasons related to the fitting of grid to the shapes of boundaries and interfaces involved. In fact, a regular grid is not suitable for problems with very steep variations of fields.

3.5.4 Finite Element Method (FEM)

The first application of finite element method appeared in 1968 when B. J. Morgan, [236] used to solve problem in wave propagation. Then P. Silvester authenticated its application in microwave engineering and electromagnetic field problems by using it for high-order wave-guide analysis [116]. The importance of the method was quickly recognized and successful applications were achieved for the analysis of a variety of electrostatic, magnetostatic and dielectric-loaded waveguide problems. However, its use and popularity in predicting field intensities in biological systems have been modest until recent progress in mesh generation, boundary conditioning and large matrix solvers. Aside from the low memory requirement, an inherent attraction of FEM is its adaptability in modeling inhomogeneities and complex geometries. The basic approach of FEM method for predicting EMF distributions inside the biological bodies starts by subdividing the physical space and biological body of interest into meshes of small volumes or cells of tetrahedral elements. Each cell element and node location is required to be systematically numbered and described. Once the volume has been subdivided, labeled, and appropriate property values ascribed, the unknown field within each element is then approximated using linear extrapolation. A major step in FEM is the formulation of the system of linear equations with proper boundary conditions that can produce an approximate solution to unknown field intensity with a prescribed accuracy [237].

3.5.5 Advantages of FEM over other Numerical Techniques

FEM models can provide users with quick, accurate solutions to multiple systems of differential equations. FEM is advantageous over other numerical approaches to obtain information near complex boundaries of the structure. The quasi-static impedance method is restricted to lower frequencies, but the MoM, the FDTD and the FEM methods may be used for any frequency of interest [238]. In addition, both FDTD and the FEM methods involve solving Maxwell's equations in the differential form for the computation of induced fields. The main advantages of FEM over other numerical techniques are:

- Very straightforward treatment of complex geometries and material inhomogeneities.
- Very simple handling of dispersive materials (i.e. materials with frequency dependent properties).
- Ability to handle Eigen value problems.
- Better frequency scaling than MoM in its basic form, although the requirement to mesh a volume rather than a surface means that the number of unknowns in the problem is usually much larger. For a typical mixed first order scheme, this has the same computational complexity as the FDTD. Depending on the problem, the number of unknowns can be lower in FEM than an FDTD solution (due to a better geometrical modeling capability of tetrahedral mesh).
- Straightforward extension to higher order basis functions, which can substantially reduce the asymptotic computational complexity due to the lower dispersion. The FEM lends itself to the use of higher order basis functions. It is also possible to use conformal elements to even better approximate curved geometries [237].

3.6 Finite Element Implementation for MWA

The basic generic steps for FEM simulation involves preprocessing, followed by solution determination and post processing as shown in Figure 3.2.

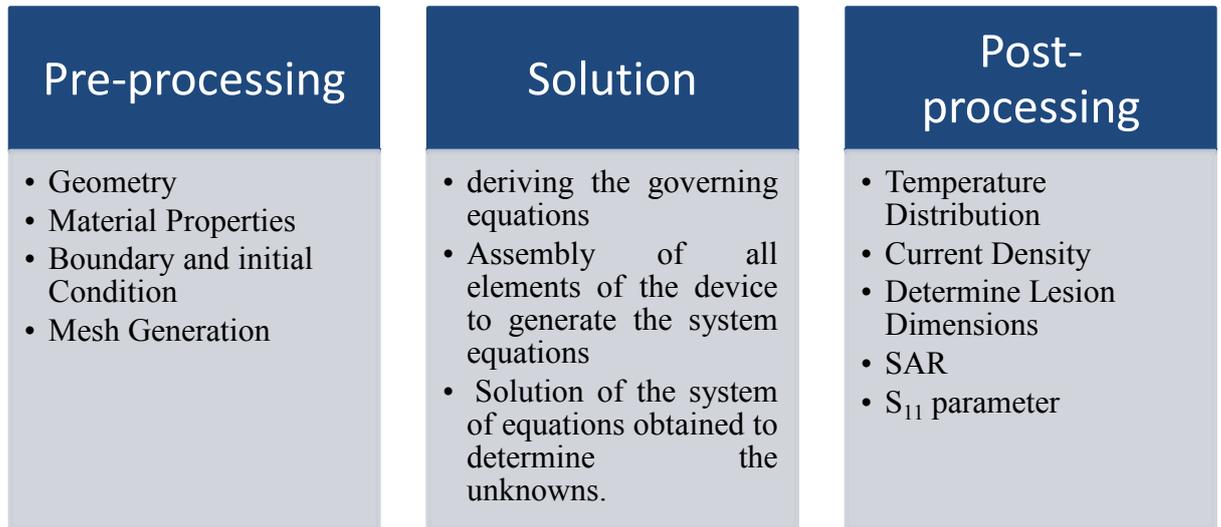


Figure 3.2 Three basic generic steps for FEM simulation

3.6.1 Preprocessing

The preprocessing stage includes the initial model generation subject to the given material properties and suitable boundary conditions. The steps involved in preprocessing stage are explained as below:

3.6.1.1 Geometric Modeling

In preprocessing stage initially geometric model of the liver is employed for computer modeling of antenna applicator during device design. The liver tissue is typically modeled as a homogenous block, ignoring the microvasculature and pores. This is likely because theoretical models are usually validated in tissue phantoms and ex-vivo models. Furthermore, the most frequently used in vivo animal model, porcine liver, does not incorporate a tumor. Most devices for HCC microwave ablation are

based on a coaxial antenna design. The antenna structure is specified in fine details so as to obtain a good approximation of its radiation pattern. The modeling of antenna/applicator is accomplished in axisymmetric geometry, which converts a 3D problem to 2D problem, to simplify the modeling and reduce complexity of computation. Axisymmetric models also used to solve Maxwell's equations and the bioheat equation [239] for cylindrically symmetric coaxial designs.

3.6.1.2 Boundary and Initial Conditions

Appropriate boundary and initial conditions need to be specified before the solution of the relevant PDEs. Initial temperature of the tissue is set to body core temperature of 37°C. The source for the electromagnetic model needs to be specified in order to launch the appropriate electromagnetic wave. For electromagnetic problem, the boundary conditions are specified as a perfectly matched layer (PML) or absorbing/low reflecting boundary condition along the edge of the tissue to simulate an infinitely large medium. This is done to prevent microwave energy reflecting back into target zone from the edge of the boundary. But in practice, this is negligible since the size of the tissue being modeled is typically larger than several penetration depths of microwaves. For thermal problem, boundary conditions along the edge of the simulation space are specified as fixed temperature of the body core, or as thermally insulating boundary conditions. In order to reduce size of the simulation, many models exclude metallic components by modeling them as perfect electric conductors (PEC). For the material with infinitely large electric conductivity, in the material the electric field goes to zero. By setting the boundary condition along the edges of all metallic parts, these components can be excluded from the computational domain. However, such types of models inherently ignore any losses in the coaxial cable structure, while these losses have little effect on the radiation pattern of the antenna, as they do not account for heating of the coaxial

cable due to conductor and dielectric losses. The observation from experimental studies shows that substantial heating of the coaxial feed-line occurs during high power microwave ablation which is due to dielectric and conductor loss in the coaxial feed-line assembly. Therefore, accurate models should account for losses in the coaxial feed-line, However, this is the most challenging task since skin depth in most good conductors used for coaxial cable (e.g. Copper) is very small, thus extremely fine spatial discretization is needed, which comes at the expense of increased computational burden. In thermal model, all metallic components are readily included within the computation domain by specifying appropriate thermal properties.

3.6.1.3 Meshing

While discretizing the computational domain, the wavelength in tissue is the governing factor for maximum node spacing. Therefore, the maximum inter-node spacing should be an order of magnitude lower than the wavelength in tissue at the frequency of operation. It is very common to use mesh element size at 1/10 to 1/8 of the wavelength. For instance, if the operating frequency is of the order of 2.45 GHz, the wavelength in liver tissue is 1.85 cm. Thus, a maximum node spacing of millimeter suffices. The finer spacing should be used at the source boundary, as well as boundaries between the antenna radiating element and the tissue. Meshes created for solution of Maxwell's equations are more than sufficiently accurate for the solution of the thermal model. Variable node spacing is usually used to focus more computational resources in critical regions (e.g. source boundary, antenna tissue interface) and use fewer resources in regions far away from the antenna. Although the above procedure works well in most cases, a Cauchy convergence test is performed to determine whether the mesh resolution and time step size are sufficiently small. This is performed by computing some objective quantity (e.g. antenna reflection coefficient, S_{11} or size of ablation zone)

using the model for increasingly finer meshes. When the change in the objective quantity due to finer mesh drops below a specified threshold, the mesh size used can be assumed to be sufficient for the problem at hand. The reflection coefficient represents how much power is reflected from the antenna, and hence is known as the reflection coefficient. If $S_{11}=0$ dB, then all the power is reflected from the antenna and nothing is radiated. If the antenna radiates best at a particular frequency, is called resonant frequency and must be approximately same as operating frequency.

3.6.2 Solution

After assigning appropriate material properties, initial conditions, boundary conditions, and meshing for the geometry, solution is generated with global equation system. The finite element global equation system is typically sparse, symmetric and positive. Direct and iterative methods can be used for solution. The nodal values of the sought function are produced as a result of the solution. Since power-controlled and temperature controlled ablation are generally used in clinical applications, resulting power, or tip temperature after each time step must be checked. If the power or the temperature is out of the target, the voltage or the current source applied to the model is adjusted. Again new parameters are submitted to solver and this process of trial and error requires long computation time.

3.6.3 Post-processing

After obtaining the solutions from the solver, almost any thermal quantities can be plotted as special distribution or temporal function. The parameters such as temperature or current density distributions are analyzed using post-processing applications.

The post processing, involves processing the data generated to obtain characteristics of interest like: reflection coefficient S_{11} , thermal lesions, temperature distribution, SAR

and resonant frequency etc. Besides plotting the field variables, boundary and volume integrations for the field variables can be done in order to calculate the values of power being delivered, reflected, deposited and leaked.

3.7 COMSOL Multiphysics

COMSOL Multiphysics 3.4 is an engineering modeling package used for the simulation of any physical process that can be described with Partial Differential Equations (PDE) [239]. The main feature of this software is its state-of-the-art solvers which addresses the complex problems quickly and accurately based on FEM. It has the ability to model coupled physics phenomena that deal with the realistic representations of the practical problems. Extensive model libraries and specific application modules provide a user friendly simulation environment. COMSOL Multiphysics 3.4 also offers an extensive interface to MATLAB and its toolboxes for a large variety of programming, preprocessing and post processing possibilities.

For numerical simulation of microwave antenna for MWA, COMSOL Multiphysics uses RF module and heat transfer module as coupled problem. The RF module characterises electromagnetic fields, currents, and waves for RF, microwave, optical and other high frequency problems. It allows for extensive post-processing such as temperature, surface heat, SAR, S-parameter computations and far-field analyses [239].

3.8 Conclusions

In this chapter, the fundamentals of bioelectromagnetics have been presented. The interaction of microwaves with tissue has been explained in view of the Maxwell equation, complex permittivity, conductivity, dielectric properties and power flow. Heat transfer in tissue, dosimetry concept, SAR definition, bioheat equation and blood perfusion and effects, thermal properties and dependent factors, thermal responses of

biological tissues during MWA have been explained for the evaluation of energy absorption on the exposed targets. Subsequently thermometry techniques for measuring temperature have been explained briefly. Several numerical computational techniques like MoM, FDTD and FEM used to solve bioelectromagnetic problems has also been discussed. Finite Element Method (FEM) has been selected in comparison to other mentioned numerical techniques, as it has been observed that FEM is the most suitable one for such quasi-static problem with curvature geometric structures, inhomogeneous material and also saves computation resources and time. This chapter describes the requirements for creating numerical models for microwave tissue ablation using FEM. Finally, commercial software package i.e. COMSOL Multiphysics 3.4, used in this research is briefly introduced.